Remarks/Arguments

Prior to submission of this amendment, claims 1-30 were pending in the application. Applicants have canceled claims 1-24 and 26-30 without prejudice to filing a continuation or divisional application directed to the canceled subject matter. Applicants have added Claims 31-44. Claims 25 and 31-44 are now pending.

1. Amendments

Support for the amendments to the specification is found throughout the specification and the claims.

In particular, the specification was amended at page 5, line 3, paragraph [0027] to correct obvious typographical errors regarding the numbering of the functional regions within the amino acid sequence of SEQ ID NO:2 as mentioned on page 5 of the specification.

This correction is necessitated by the filing of the amended Sequence Listing SEQ ID NO:2 which renumbered the amino acid sequence to begin with amino acid number +1. SEQ ID NO:2 originally filed with the PCT application had the amino acid sequence beginning with number –45.

We submit that the correct numbering of the functional regions of SEQ ID NO:2 (i.e. according to the numbering with position 1 assigned to the N-terminal methionine residue) are:
putative signal sequence – amino acids 1 to 45 of SEQ ID NO:2;
putative precursor sequence – amino acids 46 to 259 of SEQ ID NO:2;
putative soluble portion – amino acids 260 to 309 of SEQ ID NO:2; and
putative transmembrane portion: - amino acids 310 to 344 of SEQ ID NO:2.

It should be acknowledged that there are some inconsistencies in the specification as filed and in the numbering of the original SEQ ID NO:2 and the current SEQ ID NO:2. This is apparent from the numbering of the signal sequence to positions 1 to 45 at page 5 of the specification, but the numbering of signal sequence in the original SEQ ID NO:2 starting with

position –45. It is understood by one skilled in the art that signal sequences are generally present in the N-terminus of a secreted or membrane bound protein. Thus it would be immediately evident to a skilled person that the allocation of positions 1 to 45 refers to an amino acid sequence the numbering of which starts with +1 and not with –45. It would therefore have been obvious that there is a typographical error.

Further items that would lead a skilled person to conclude that the annotations on page 5 of the description as filed are incorrect, are for example, the transmembrane portion is ascribed to amino acid positions 264 to 344. However, the numbering of SEQ ID NO:2 as originally filed ends at position 329.

Thus one skilled in the art would look to the specification to arrive at the correct functional regions. As discussed above, using SEQ ID NO:2 commencing with methionine as amino acid +1, one skilled in the art would recognize that the signal sequence region was from amino acids 1 to 45. One skilled in the art would also recognize that the entire amino acid sequence would be amino acids 1 to 374.

Concerning the putative soluble region (amino acids 260 to 309 of SEQ ID NO:2) a skilled person would look to Example 2. Specifically on page 240, paragraph [0146] it is described that by use of the primers having the nucleotide sequences depicted under SEQ ID NO:9 and 10, a construct encoding the putative soluble portion can be amplified. This construct is indicated to range from nucleotide 1100 to 1248 of SEQ ID NO:1. A comparison of this nucleotide sequence with that shown in Figure 1 reveals that this nucleotide sequence exactly encodes amino acids 260 to 309 of the amino acid sequence given in Figure 1 (if this sequence is numbered beginning with +1, according to corrected SEQ ID NO:2). Applicants note that position 309 in SEQ ID NO:2 (methionine as position +1) corresponds to amino acid 264 in the original SEQ ID NO:2.

Concerning the putative precursor region, (amino acids 46 to 259 of SEQ ID NO:2), a person skilled in the art given the understanding of the soluble region would understand from the paragraph at page 5 that the precursor region is followed by the soluble region. Thus a person skilled in the art would derive that the precursor region ranged from position 46 to position 259 of SEQ ID NO:2. Applicants note that position 259 in SEQ ID NO:2 (methionine as position +1) corresponds to amino acid 214 in the original SEQ ID NO:2.

Concerning the putative transmembrane region (amino acids 310 to 344 of SEQ ID NO:2) the C-terminus of this region is correctly stated on page 5. A skilled reader would not doubt this because this position does not conflict with the other sequence ranges and the renumbering of SEQ ID NO:2 gives the value 344 a reasonable meaning. Regarding the N-terminus of this region, a skilled reader would understand from page 5 that the transmembrane region follows the soluble region and thus the N-terminus would be amino acid 310.

From the forgoing it is clear that the requested re-numbering of the annotations for the functional regions of SEQ ID NO:2 in the specification find a basis in the application as filed. Entry of the amendment to the specification is respectfully requested.

Claim 25 has been amended to recite a method for the treatment of a patient having need to inhibit TGFα-HII comprising: administering to the patient a therapeutically effective amount of an antibody capable of binding to a polypeptide comprising a member selected from the group consisting of various recited amino acids sequences. Support for the antibody can be found, for example, in the specification and in original claim 21. Support for the various recited amino acid sequences can be found, for example, in the specification and in original claim 19. The ranges of the functional regions of SEQ ID NO: 2 have been amended to be consistent with the amendments to the specification discussed above.

New claims 31 – 44 are presented herein. Support for the newly added claims is found throughout the specification and claims as originally filed. In particular, support for newly added claims 31 – 44 can be found in the specification at, for example, page 26, line 7, paragraph [0127] to page 36.

2. Restriction Requirement

The PTO requires the restriction of the claims in the above-identified application into one of the following 10 groups of claims.

I. Claims 1-20 drawn to nucleic acids and polypeptides.

II. Claim 21, drawn to an antibody.

III. Claim 22, drawn to inhibitory compounds.

IV. Claim 23, drawn to receptor activating compounds.

V. Claim 24, drawn to a method of treatment by administering the protein.

VI. Claim 25, drawn to a method of treatment by administering the inhibitory compound.

VII. Claim 26, drawn to a method of treatment by administering the nucleic acid.

VIII. Claims 27-28, drawn to a method for identifying compounds.

IX. Claim 29, drawn to a method of diagnosis using nucleic acid sequences.

X. Claim 30, drawn to a method of diagnosis using the protein.

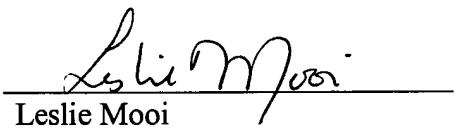
Applicant elects for examination the claims of Group VI, claim 25 drawn to a method of treatment by administering the inhibitory compound. This election is made without traverse.

Please direct any calls in connection with this application to the undersigned at the number provided below.

Please charge any additional fees, including additional fees for extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39766-0151US D2).

Respectfully submitted,

Date: June 12, 2006



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